

BIOGRAPHICAL SKETCH

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NAME: Lee, Hye Young, PhD

eRA COMMONS USER NAME (credential, e.g., agency login): HYELEE

POSITION TITLE: Assistant Professor, Department of Cellular and Integrated Physiology

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
EWHA Women's College, Seoul, Korea	B.S.	02/2001	Biological Sciences
POSTECH, Pohang, Korea	Ph.D.	02/2006	Signal transduction
University of California, San Francisco	Postdoctoral Fellowship	02/2013	Neuroscience

A. Positions and Honors**Positions and Employment**

2006 – 2008	Postdoctoral fellow (Signal Transduction Lab), Pohang University of Science and Technology, Pohang, Republic of Korea
2008 – 2013	Postdoctoral fellow (Lily Jan Lab), University of California, San Francisco, CA
2013 – 2016	Associate Specialist (Lily Jan Lab), University of California, San Francisco, CA
2016 – present	Assistant Professor, Department of Cellular and Integrated Physiology, UT Health San Antonio, TX

Honors

2006	Travel award: American Society for Biochemistry and Molecular Biology
2008	Fellowship, National Research Foundation of Korea
2010	Travel award: Cold Spring Harbor meeting in Suzhou, China
2011	Association of Korean Neuroscientists Outstanding Research Award
2011	Notable Korean Scientists, Korea
2012	Poster Award, Korean Life Scientist symposium, San Francisco, CA
2012	Poster Award, Neuroscience retreat, Asilomar, CA
2013	Notable Korean Scientists, Korea
2014	Schwarz Foundation travel award: Cold Spring Harbor, NY
2016	Bay Area Autism Consortium travel award, San Francisco, CA

B. Contribution to Science

1. During my PhD research, I studied the cell signaling mechanisms in various cell types, including neurons. Using mass spectrometric and proteomic approaches, I found binding proteins of phospholipase D and studied the in vitro and cell-based protein interactions and signal transduction in cells.

- a. **Lee HY**, Park JB, Jang IH, Chae YC, Kim JH, Kim IS, Suh PG, Ryu SH. (Munc-18-1 inhibits phospholipase D activity by direct interaction in an epidermal growth factor-reversible manner. J Biol Chem. 2004; 279: 16339-16348. PMID: 14744865.

- b. **Lee HY**, Lee BD, Chae YC, Kim HS, Kim SH, Cho JH, Jin CJ, Koh DS, Park KS, Suh PG, Ryu SH. Epidermal growth factor increases insulin secretion through phospholipase D2 activation. J Cell Mol Med. 2007; 12: 1593-1604. PMID: 18053093.
 - c. **Lee HY**, Jung H, Jang IH, Suh PG, Ryu SH. Cdk5 phosphorylates PLD2 to mediate EGF-dependent insulin secretion. Cell Signal. 2008; 20: 1787-1794. PMID: 18625302.
 - d. Ryu SH, Suh PG, Kim JH, Jang IH, **Lee HY**, Chae YC, Ha SH, Park JB, Kim JH, Lee SM, Lee JS, Lee CS, Kim HW, Kim IS, Jeo HA. Peptide complexes containing phospholipase D. PCT/KR03/01903 – Korean Patent, September 18, 2003.
- 2. *Using my biochemical and cellular research background, I worked with ion channel proteins and identified the dimerization domain of TMEM16A, a calcium-activated chloride channel, during my post-doc in Lily Jan's lab.***
- a. Tien J, **Lee HY**, Minor, DL Jr., Jan YN, Jan LY. Identification of a dimerization domain in the TMEM16A calcium-activated chloride channel. Proc Natl Acad Sci U S A. 2013; 110: 6352-6357. PMID: 23576756
- 3. *I discovered that the mRNA of the voltage-gated potassium channel Kv4.2 resides in neuronal dendrites and its local translation in dendrites is suppressed by the fragile X mental retardation protein linked to fragile X syndrome – the most common form of heritable mental retardation with elevated risk for autism.***
- a. **Lee HY**, Ge W, Huang W, He Y, Wang G, Rowson-Baldwin A, Smith SJ, Jan YN, Jan LY. Bidirectional regulation of Kv4.2 voltage-gated potassium channels on neuronal dendrites by fragile X mental retardation protein. Neuron. 2011; 72: 630-642. PMID: 22099464.
 - b. **Lee HY**, Jan LY. Fragile X syndrome: mechanistic insights and therapeutic avenues regarding the role of potassium channels. Curr Opin Neurobiol. 2012; 22: 887-894. PMID: 22483378.
- 4. *I have extensive experience working with fmr1 knockout (KO) mice and Kv4.2 KO mice, and have set up the genetic crosses between these lines to test our proof-of-principle hypothesis that a 50% reduction of Kv4.2 expression could rescue autistic behaviors of the fmr1 KO mutant phenotypes. A first-authored manuscript is currently in preparation.***
- 5. *I have a collaborative project with Niren Murthy lab in UC Berkeley. We developed a new delivery method of CRISPR/Cas9 in vivo and tested this new delivery method in mouse brains. A corresponding manuscript is currently under the revision.***
- a. Lee K, Lee B, Mackley V, Murthy N, **Lee HY (corresponding author)**. Non-viral gene editing in the mouse brain with CRISPR/Cas9 and Cpf1. Nature Biomedical Engineering (under the revision)

C. Publications (in chronological order)

1. Park, J. B., Lee, C. S., **Lee, H. Y.**, Kim, I. S., Lee, B. D., Jang, I. H., Jung, Y. W., Oh, Y. S., Han, M. Y., Jensen, O. N., Roepstorff, P., Suh, P. G. and Ryu, S. H. (2004) Regulation of phospholipase D2 by GTP-dependent interaction with dynamin. Adv. Enzyme Regul. 44: 249-264. PMID: 15581494.
2. **Lee, H. Y.**, Park, J. B., Jang, I. H., Chae, Y. C., Kim, J. H. Kim, I. S., Suh, P. G. and Ryu, S. H. (2004) Munc-18-1 inhibits phospholipase D activity by direct interaction in an epidermal growth factor-reversible manner. J. Biol. Chem. 279: 16339-16348. PMID: 14744865.
3. Chae, Y. C., Lee, S., **Lee, H. Y.**, Heo, K., Kim, J. H., Kim, J. H., Suh, P. G. and Ryu, S. H. (2005) Inhibition of muscarinic receptor-linked phospholipase D activation by association with tubulin. J. Biol. Chem. 280: 3723-3730. PMID: 15548524.
4. Kim, H. S., Yumkham, S., **Lee, H. Y.**, Cho, J. H., Kim, M. H., Koh, D. S., Ryu, S. H. and Suh, P. G. (2005) C-terminal part of AgRP stimulates insulin secretion through calcium release in pancreatic beta Rin5mf cells. Neuropeptides 39: 385-393. PMID: 15978665.

5. Lee, C. S., Kim, I. S., Park, J. B., Lee, M. N., **Lee, H. Y.**, Suh, P. G. and Ryu, S. H. (2006) The phox homology domain of phospholipase D activates dynamin GTPase activity and accelerates EGFR endocytosis. *Nat. Cell Biol.* 8: 477-484. PMID: 16622417. PMID: 16622417.
6. **Lee, H. Y.**, Lee, B. D., Chae, Y. C., Kim, H. S., Kim, S. H., Cho, J. H., Jin, C. J., Koh, D. S., Park, K. S., Suh, P. G. and Ryu, S. H. (2007) Epidermal growth factor increases insulin secretion through phospholipase D2 activation. *J. Cell. Mol. Med.* 12: 1593-1604. PMID: 18053093.
7. Chae, Y. C., Kim, K. L., Kim, H. W., Kim, J. H., **Lee, H. Y.**, Suh, P. G. and Ryu, S. H. (2008) Phospholipase D Activity regulates integrin-mediated cell spreading and migration by inducing GTP-Rac translocation to the plasma membrane. *Mol Biol Cell.* 19: 3111-3123. PMID: 18480413.
8. **Lee, H. Y.**, Jung, H., Jang, I. H., Suh, P. G. and Ryu, S. H. (2008) Cdk5 phosphorylates PLD2 to mediate EGF-dependent insulin secretion. *Cell Signal.* 20: 1787-1794. PMID: 18625302.
9. Kim, I. H., **Lee, H. Y.**, Lee, H. D., Jung, Y. J., Ryu, S. H. and Park, J. W. (2009) Interaction between signal transducing proteins measured by picroforce atomic force microscopy. *Analytical Chemistry.* 81: 3276-3284. PMID: 19323535.
10. Lee, S. B., Bagley, J. A., **Lee, H. Y.**, Jan, L. Y. and Jan, Y. N. (2011) Pathogenic polyQ proteins cause dendrite defects associated with specific actin cytoskeletal alterations in *Drosophila*. *PNAS.* 108: 16795-16800. PMID: 21930920
11. **Lee, H. Y.**, Ge, W., Huang, W., He, Y., Wang, G., Rowson-Baldwin, A., Smith, S. J., Jan, Y. N. and Jan, L. Y. (2011) Bidirectional regulation of Kv4.2 voltage-gated potassium channels on neuronal dendrites by fragile X mental retardation protein (FMRP). *Neuron* 72: 630-642. PMID: 22099464.
12. Yang, S. B., **Lee, H. Y.**, Young, D. M., Tien, A. C., Rowson-Baldwin, A., Shu, Y., Jan, Y. N. and Jan, L. Y. (2012) Rapamycin induces glucose intolerance in mice by reducing islet mass, insulin content and insulin sensitivity. *Journal Molecular Medicine* 90: 575-585. PMID: 22105852.
13. **Lee, H. Y.**, Jan, L. Y. (2012) Fragile X syndrome: mechanistic insights and therapeutic avenues regarding the role of potassium channels. *Curr. Opin. Neurobiol.* 22: 887-894. PMID: 22483378.
14. Tien, J., **Lee, H. Y.** (* **These authors contributed equally to this work**), Minor, Jr., D.L., Jan, Y. N. and Jan, L. Y. (2013) Identification of a Dimerization Domain in the TMEM16A Calcium-Activated Chloride Channel (CaCC). *PNAS* 110: 6352-6357. PMID: 23576756
15. Gorczyca, D., Younger, S., Song, W., **Lee, H. Y.**, Jan, L. Y. and Jan, Y. N. (2014) Identification of Ppk26, a novel DEG/ENaC channel functioning with Ppk1 in a mutually dependent manner to guide locomotion behavior in *Drosophila*. *Cell Report* 9:1446-58. PMID: 25456135
16. **Lee, H. Y.**, Jung, S. Y., Kim, J. H., Suh, P. G. and Ryu, S. H. Phospholipase D2 regulates dendritic spine morphogenesis and synaptic activity. *PLoS One* (in revision).
17. **Lee, H. Y.**, Jan, Y. N., Jan, L. Y. Reversing the autistic-like phenotypes in *fmr1* KO mice by genetic reduction of Kv4.2 potassium channels. (in preparation)
18. Lee, K., Lee, B., Mackley, V., Murthy, N., **Lee, H. Y.** Non-viral gene editing in the mouse brain with CRISPR/Cas9 and Cpf1 (submitted and under the review in *Nature Biomedical Engineering*), as a corresponding author

D. Research Support

Ongoing Research Support

#P0054266 Lee (PI) 01/15/2014-01/14/18
 Brain and Behavior Research Foundation (NARSAD)
 Evaluation of Kv4.2 Potassium Channels as Potential Therapeutic Targets for Fragile X Syndrome
 A Young Investigator award.
 Role: PI

San Antonio Life Sciences Institute (SALSI) Academy 06/01/2016-05/31/2017
 Elucidating Social Communication Deficits in Autism
 Role: PI

IIMS-CTSA/CBN Pilot 02/01/2017-01/31/2018
 Cellular and Functional Role of Microglia in Fragile X Syndrome
 Role: PI

**Exciting projects are waiting for Xiangya medical students (up to two persons)
in Lee lab at UT Health San Antonio**

The Lee lab studies the molecular neurobiology and the etiology of autism and related neuropsychiatric disorders, using a range of cutting-edge molecular, cellular and integrative approaches. Autism spectrum disorders (ASD) form a heterogeneous neurodevelopmental syndrome characterized by deficits in language development/social interactions, and repetitive behavior/restricted interests. ASD likely arises from a complex combination of risk factors. However, it remains possible that certain aspects of the molecular pathophysiology responsible for ASD are recurrent themes that can inform the underlying neurobiological basis of ASD.

The Lee lab focuses on: **1)** identifying the molecular mechanisms responsible for the pathophysiology of autism and related disorders, and using these mechanisms to rescue behavioral dysfunction in mouse models, and **2)** elucidating specific autistic behaviors including social communication deficits and repetitive behaviors, and identifying the brain region(s) and neuron groups underlying these behavioral deficits in mouse models. To address these questions, **we use molecular and cellular neurobiology tools, *in vivo* brain imaging, and animal behavioral studies.** Individuals with research experience or interest in these questions who are self-motivated with a passion for autism research are encouraged to apply. Applicants are encouraged to view the recent publications and related review papers of Dr. Lee, who trained with Lily Jan at UCSF.

Two positions are available in the Lee lab for those who are interested in joining these following projects:

1. Identification of the molecular and cellular mechanisms responsible for fragile X syndrome
2. Developing therapeutic treatments for fragile X syndrome or related disorders

San Antonio, the 7th largest city in the nation, is a diverse, multicultural city with much to offer including an attractive cost-of-living. The University of Texas Health Science Center at San Antonio is a highly research-oriented medical center with focus in multiple areas of research, with neuroscience a leading focus. The Department of Physiology boasts fifteen active laboratories performing neuroscience research. For any question, please feel free to contact Hye Young Lee at leeh6@uthscsa.edu.